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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/752,415

01/06/2004

Bellon Laurent

MBHB00-885-E; 600.040

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09/19/2007

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EXAMINER

PITRAK, JENNIFER S

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

09/19/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/752,415	Applicant(s) LAURENT ET AL.	
	Examiner Jennifer Pitrak	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments and Amendments

Applicant's arguments, see remarks on p.6 and amended Claims 8 and 9, filed 06/28/07, with respect to the rejection under 35 U.S.C. § 112, second paragraph as being indefinite have been fully considered and are persuasive. Claims 8 and 9 have been amended to properly depend from Claim 7. The rejection of claims 8 and 9 has been withdrawn.

Claim Rejections - Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 14 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, and 12 of U.S. Patent No. 6,054,576 in view of Usman, *et*

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al. (BQ, 01/06/04 IDS). This rejection is maintained for the reasons of record (see p.5 of 03/15/07 Office Action).

Claim 15 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, and 12 of U.S. Patent No. 6,054,576 in view of Usman, *et al.* (BO, 01/06/04 IDS). This rejection is maintained for the reasons of record (see p.5 of 03/15/07 Office Action). Applicants have not provided any arguments, evidence, or a terminal disclaimer that addresses this rejection. Normally, this would render the response non-compliant. However, in the interest of compact prosecution, applicants are merely reminded that a complete response requires applicant to respond to all rejections of record.

Claim Objections and Rejections - New

Claim Objections

Claims 18-22, 24, and 28 are objected to under 37 CFR 1.75 as being substantial duplicates of claims 7-11, 23, and 27. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-22, 25, and 26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Stinchcomb, *et al.* (WO95/23225 – item AI of 01/06/04 IDS).

The claims are to a process for synthesis, deprotection, and purification of an RNA molecule comprising solid phase synthesis, one-pot deprotection, and purification, wherein deprotection comprises contacting protected RNA with a mixture of an alkylamine and a polar organic reagent for cleavage of RNA from a solid support and removal of base and phosphate protecting groups, and contacting the RNA with triethylamine-hydrogen fluoride for removal of a 2'-OH-protecting group (claim 1), wherein RNA purification comprises HPLC purification including reverse phase or ion-exchange chromatography (claims 2-4), wherein the RNA comprises trialkylsilyl protecting groups (claim 5) including tert-butyl dimethylsilyl protecting groups (claim 6), and wherein the alkylamine comprises methylamine (claims 11 and 22). The claims are further directed to the process of claim 1 wherein the RNA comprises modified nucleotides (claims 7 and 18), wherein the modified nucleotides comprise 2'-deoxy-2'-fluoro (claims 8 and 19), 2'-O-methyl (claims 9 and 20), or 2'-deoxy (claims 10 and 21) nucleotides. The claims are further directed to the process of claim 1 wherein the solid phase synthesis uses polystyrene (claim 13), wherein the phosphate protecting groups comprise cyanoethyl protecting groups (claim 14), wherein the base protecting groups comprise N-acetyl, N-benzoyl, or N-isobutyryl protecting groups (claim 15), and wherein the RNA comprises one or more modified internucleotide linkages (claim 16). The claims are further directed to the process of claims 1 and 18 wherein the RNA is contacted with triethylamine-hydrogen fluoride at about 50-70 degrees Celsius (claims 25 and 26).

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Stinchcomb, *et al.* teach a one-pot protocol for RNA deprotection wherein solid phase-synthesized protected RNA is deprotected on a one-pot fashion with a mixture of anhydrous methylamine in absolute ethanol (a polar organic reagent) followed by neat triethylamine trihydrofluoride as described in Figure 12 of Stinchcomb, *et al.* and in the instant specification (bottom of p.2). Stinchcomb, *et al.* teach tert-butyl dimethylsilyl-protected RNA (pp. 77, lines 25-29) and RNA comprising 2'-fluoro, 2'-deoxy, and 2'-O'-methyl nucleotides (p. 23, lines 10-15) as well as purification of the RNA by reverse phase or anion-exchange chromatography (p.67, lines 26-28). Stinchcomb, *et al.* also teach the RNA synthesis on polystyrene or controlled pore glass (p.149, example 95); cyanoethyl phosphate protecting groups (Figure 75 and p.18); N-acetyl, N-benzoyl, and N-isobutyryl nucleic acid base protecting groups (Figure 8 and p.64); phosphorothioate internucleotide linkages (Figure 15 and p.9); and removal of the alkylsilyl protecting groups with anhydrous triethylamine-hydrofluoride at 65 degrees C (p. 67, lines 4-8).

Thus, Stinchcomb, *et al.* anticipate all of claims 1-22, 25, and 26.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stinchcomb, *et al.*, as applied to claims 1-22, 25, and 26 above, and further in view of Gasparutto, *et al.* (1992. Item AS on 01/06/04 IDS) and Woo, *et al.* (1990. US Patent 4,965,349).

The claims are to the process of RNA synthesis, deprotection, and purification as described above for claim 1, wherein the RNA is contacted with the mixture of alkylamine and polar organic reagent in predetermined proportions at room temperature for about 30 to about 100 minutes (claims 23 and 24) or wherein the polar organic reagent is DMSO (claims 27 and 28).

Stinchcomb, *et al.* teach the solid phase RNA synthesis and deprotection with an alkylamine in a polar organic reagent as described above. Stinchcomb, *et al.* do not teach the polar organic reagent DMSO. Stinchcomb, *et al.* do not teach contacting RNA with the mixture of alkylamine and polar organic reagent in predetermined proportions at room temperature for about 30 to about 100 minutes.

Gasparutto, *et al.* teach the use of DMSO with TBAF for RNA deprotection as an improvement to RNA deprotection because it facilitated RNA solubility (p.5161, first column). Woo, *et al.* teach cleavage and deprotection of RNA at room temperature for longer time periods as an alternative to shorter time periods at higher temperatures (paragraph bridging columns 6 and 7).

It would have been obvious to one skilled in the art at the time of the invention to use DMSO as the polar organic reagent in RNA deprotection because Gasparutto, *et al.* teach improved RNA deprotection with the use of DMSO. Furthermore, one would expect successful

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deprotection of RNA at room temperature for about 30 to about 100 minutes given the disclosure of Woo, *et al.* as described above.

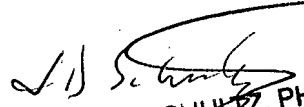
Closing

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSP


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SUPERVISORY PATENT EXAMINER